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L7: Entry 19 of 33 File: USPT

DOCUMENT-IDENTIFIER: US 6074666 A
TITLE: Liposome compositions of porphyrin photosensitizers

Brief Summary Text (2):
The invention relates to improved pharmaceutical formulations comprising liposomes incorporating porphyrin photosensitizers. Specifically, the invention is directed to a freeze-dried pharmaceutical formulation comprised of a porphyrin photosensitizer, a disaccharide or polysaccharide and one or more phospholipids which, upon reconstitution with a suitable aqueous vehicle, forms liposomes containing the porphyrin photosensitizer. Particular porphyrin photosensitizers which are advantageously employed in the practice of this invention include the hydro-monobenzoporphyrins having a light absorption maxima in the range of 670-780 nanometers. The photosensitizing formulations are useful to mediate the destruction of unwanted cells or tissues or other undesirable materials by irradiation or to detect their presence through flourescence.

Brief Summary Text (11):
In an effort to increase the tumor selectivity of porphyrin photosensitizers, the porphyrin compounds have been incorporated into unilamellar liposomes resulting in a larger accumulation and more prolonged retention of the photosensitizer by both cultured malignant cells and experimental tumors in vivo. Jori et al., Br. J. Cancer, (1983) 48: 307-309; Cozzani et al., In Porphyrins in Tumor Phototherapy, Andreoni et al., eds., (1984) pp. 177-183, Plenum Press. The more efficient targeting of tumor tissues by liposome-associated porphyrins may be partly due to the specific delivery of the phospholipid vesicles to serum lipoproteins, which have been shown to interact preferentially with hyperproliferative tissue such as tumors through receptor mediated endocytosis. In this manner the selectivity of porphyrin uptake by tumors is increased as compared with photosensitizers dissolved in aqueous solution. See Zhou et al., supra.

Brief Summary Text (15):
The present invention involves a freeze dried pharmaceutical formulation comprising a porphyrin photosensitizer, a disaccharide or polysaccharide, and one or more phospholipids, which freeze-dried formulation forms liposomes containing a therapeutically effective amount of the porphyrin photosensitizer upon reconstitution with a suitable aqueous vehicle. The invention also relates to the liposome composition formed upon reconstitution with said aqueous vehicle.

Brief Summary Text (26):
The liposomes of the present invention possess certain attributes which make them particularly suited for delivering the porphyrin photosensitizers. Conventional liposomal formulations are preferentially taken up by the reticuloendothelial system (RES) organs such as the liver and spleen. When this occurs, the major portion of the liposomal encapsulated water insoluble drug is not available to tumor sites since it is localized in the RES. In contrast, the liposomes formed in the present invention are "fast breaking" in that the drug-liposome combination is stable in vitro but when administered in vivo, the photosensitizer is rapidly released into the bloodstream where it associates with serum lipoproteins. It is believed that this inhibits the drug from being accumulated in non-target tissues such as the liver, where liposomes otherwise have a tendency to concentrate. The "fast breaking" nature of the present liposomes may be due to the manner in which the porphyrin photosensitizer associates with the lipid bilayer of the liposomes of the present invention.

Detailed Description Text (2):
The present invention relates to a pharmaceutical liposome formulation of a porphyrin photosensitizer for use in the photodynamic therapy or diagnosis of tumors, or for a variety of other therapeutic applications. The liposomes are formed upon addition of an aqueous vehicle to a freeze-dried formulation of a porphyrin photosensitizer, a disaccharide or polysaccharide, and one or more phospholipids such as phosphatidyl cholines or phosphatidyl glycerols. The presence of the disaccharide or polysaccharide in the formulation yields liposomes which have extremely small and narrow particle size, in which the porphyrin photosensitizers may be stably incorporated into the liposome in an efficient manner with encapsulation efficiency approaching 80-100% of the drug. The liposomes exhibit physical and chemical stability such that they retain incorporated porphyrin drugs without leakage upon prolonged storage, as either a reconstituted liposomal suspension or cryodesiccated powder. For example, BPD-MA, a preferred porphyrin photosensitizer, maintained its potency in the cryodesiccated liposome formulation for a period of at least nine months at room temperature and had a projected shelf life of at least two years.

Detailed Description Text (4):
Liposomes containing a selected porphyrin photosensitizer as described herein may be prepared by dissolving the porphyrin photosensitizer, the phospholipids and other optional adjuvants such as antioxidants in methylene chloride or other suitable organic solvents. The resulting solution is dried under vacuum until the organic solvent is evaporated. The solid residue is dispersed in an aqueous solution of the disaccharide or polysaccharide and homogenized. The solution is then freeze dried for storage and reconstituted prior to administration with a suitable aqueous vehicle such as sterile water for injection. Upon reconstitution, liposomes are formed which incorporate a therapeutically effective amount of the porphyrin photosensitizer.

Detailed Description Text (10):
The use of these porphyrin photosensitizers incorporated in liposomes for the treatment or diagnosis of cancer is described herein as a new effective treatment or therapeutic method. The liposomal formulations are useful in sensitizing neoplastic cells or other abnormal tissue including infectious agents to destruction by exposure to light using preferably, visible light. Upon photoactivation, the porphyrin photosensitizer promote the formation of singlet oxygen which is responsible for the cytotoxic effect. In addition, the porphyrin photosensitizers, when photoactivated, will fluoresce when subjected to appropriate excitation wavelengths. This fluorescence can be used to localize the tumor or other target tissue. By incorporating the porphyrin photosensitizer in the liposomes of the present invention, more efficient sensitization of tumor tissues can be obtained.

Detailed Description Text (11):
Generally speaking, the concentration of the porphyrin photosensitizer in the liposome depends upon the nature of the photosensitizer used. When the benzoporphyrin derivatives such as BPD-MA are used, the photosensitizer is incorporated in the liposomes at a concentration of about 0.10% up to 0.5% w/v, yielding a reconstituted solution of up to 5.0 mg/ml.

Detailed Description Text (13):
The quantity of photosensitizer liposome formulations to be administered depends on the choice of active ingredients, the conditions to be treated, the mode of administration, the individual subject and the judgement of the practitioner. Generally speaking, dosages in the range of 0.05-10 mg/kg may be needed. The foregoing range is of course merely suggestive, as the number of variables in regard to an individual treatment regime is large and considerable excursions from these recommended values are expected.

Detailed Description Text (18):
Either unilamellar or multilamellar or other types of liposomes may be used in the practice of the present invention. They may be prepared in a suspension form or may be formed upon reconstitution of a lyophilized powder containing the porphyrin--phospholipid--saccharide composition with an aqueous solution.

Detailed Description Text (19):

These following examples are presented to describe preferred embodiments, utilities and attributes of the present invention but are not meant to limit the invention. For example, although DMPC and EPG were used to form liposomes, these particular phospholipids are by no means the only available usable lipid forms known to those skilled in the art. Nor do the particular methods of forming or preparing the liposomes described herein constitute the only methods for preparing liposomes contemplated by the present invention. Moreover, although the examples imply the photosensitizer BPD-MA, the procedures, results and preparations should be similar for other porphyrin photosensitizers.

End of Result Set

L11: Entry 5 of 5 File: EPAB Feb 14, 1995

DOCUMENT-IDENTIFIER: US 5389378 A
TITLE: Benzoporphyrin vesicles and their use in photodynamic therapy

Abstract (1):
This invention relates to benzoporphyrin containing vesicles which are suitable for pharmaceutical application. In particular, the present invention relates to a liposomal preparation of benzoporphyrin (BPD) incorporated into vesicles comprising a liposome forming lipid such as EPC or DMPC at a drug to lipid ratio of greater than 100 mu g/umole lipid which will allow adequate drug dosing with relatively low lipid concentration. In an additional aspect of the present invention, sized liposomes are described which are storage stable. Certain sized BPD-containing vesicles (no greater than about 120 nm in diameter) permit sterilization by terminal filtration. Further, a lyophilized preparation of the BPD-lipid mixture can be obtained from aqueous buffer under conditions which do not result in vesicle fusion/aggregation or BPD precipitation. Liposomes according to the present invention are able to accommodate surprisingly large amounts of BPD within the bilayer of the liposome, rather than in the encapsulated buffer. The advantages of this surprising aspect of the present invention includes the ease of manufacture and the cost savings associated with an efficient use of BPD are also presented.

L11: Entry 3 of 5 File: USPT

DOCUMENT-IDENTIFIER: US 5616342 A
TITLE: Emulsioin suitable for administering a poorly water-soluble photosensitizing compound and use thereof

Brief Summary Text (10):
Several liposomal porphyrin formulations are in human clinical trials. These include benzoporphyrin derivative (Quadra Logic Technologies, Inc., Vancouver, B.C., Canada) and Zn-phthalocyanine (CIBA-GEIGY Ltd., Basel, Switzerland). Liposomes are submicron, hollow vesicles consisting of hydrated, synthetic phospholipids arranged in a bilayer structure. However, to the best of applicant's knowledge, there are no heat-stable oil-in-water emulsions available that are suitable for injecting poorly water-soluble photosensitizing drugs. An oil-in-water emulsion is a microscopic dispersion of oil droplets in a continuous aqueous phase with a surfactant used to stabilize the dispersed droplets.

Brief Summary Text (16):
Liposomal formulations are not especially storage stable unless lyophilized. The liposomal formulations are very sensitive to light since the suspensions are translucent.

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☐ 1. Document ID: US 6176842 B1

L11: Entry 1 of 5 File: USPT

US-PAT-NO: 6176842
DOCUMENT-IDENTIFIER: US 6176842 B1

TITLE: Ultrasound assembly for use with light activated drugs

DATE-ISSUED: January 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tachibana; Katsuro	Fukuoka			JP
Tachibana; Shunro	Fukuoka			JP
Anderson; James R.	Redmond	WA		
Lichttenegger; Gary	Woodinville	WA		

US-CL-CURRENT: 604/22; 604/101.03, 604/102.03, 604/103.01

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

☐ 2. Document ID: US 6074666 A

L11: Entry 2 of 5 File: USPT

US-PAT-NO: 6074666
DOCUMENT-IDENTIFIER: US 6074666 A

TITLE: Liposome compositions of porphyrin photosensitizers

DATE-ISSUED: June 13, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Desai; Narendra Raghunathji	Danbury	CT		
Agha; Bushra J.	Durham	NC		
Kale; Kalidas Madhavrao	Harriman	NY		

US-CL-CURRENT: 424/450

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

☐ 3. Document ID: US 5616342 A

L11: Entry 3 of 5 File: USPT

US-PAT-NO: 5616342
DOCUMENT-IDENTIFIER: US 5616342 A

TITLE: Emulsioin suitable for administering a poorly water-soluble photosensitizing compound and use thereof

DATE-ISSUED: April 1, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lyons; Robert T.	Cary	NC		

US-CL-CURRENT: 424/450; 514/410

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

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☐ 4. Document ID: US 5389378 A

L11: Entry 4 of 5 File: USPT

US-PAT-NO: 5389378
DOCUMENT-IDENTIFIER: US 5389378 A

TITLE: Benzoporphyrin vesicles and their use in photodynamic therapy

DATE-ISSUED: February 14, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Madden; Thomas D.	Vancouver			CA

US-CL-CURRENT: 424/450; 428/402.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

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☐ 5. Document ID: US 5389378 A

L11: Entry 5 of 5 File: EPAB Feb 14, 1995

PUB-NO: US005389378A
DOCUMENT-IDENTIFIER: US 5389378 A
TITLE: Benzoporphyrin vesicles and their use in photodynamic therapy

PUBN-DATE: February 14, 1995

INVENTOR-INFORMATION:

NAME	COUNTRY
MADDEN, THOMAS D	CA

INT-CL (IPC): A61 K 9/127
EUR-CL (EPC): A61K009/127; A61K031/40

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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Terms	Documents
L10 and (dehydrat$ or lyophiliz$)	5

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☐ 1. Document ID: US 6176842 B1

L12: Entry 1 of 4 File: USPT

US-PAT-NO: 6176842
DOCUMENT-IDENTIFIER: US 6176842 B1

TITLE: Ultrasound assembly for use with light activated drugs

DATE-ISSUED: January 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tachibana; Katsuro	Fukuoka			JP
Tachibana; Shunro	Fukuoka			JP
Anderson; James R.	Redmond	WA		
Lichttenegger; Gary	Woodinville	WA		

US-CL-CURRENT: 604/22; 604/101.03, 604/102.03, 604/103.01

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6074666 A

L12: Entry 2 of 4 File: USPT

US-PAT-NO: 6074666
DOCUMENT-IDENTIFIER: US 6074666 A

TITLE: Liposome compositions of porphyrin photosensitizers

DATE-ISSUED: June 13, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Desai; Narendra Raghunathji	Danbury	CT		
Agha; Bushra J.	Durham	NC		
Kale; Kalidas Madhavrao	Harriman	NY		

US-CL-CURRENT: 424/450

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 3. Document ID: US 5616342 A

L12: Entry 3 of 4 File: USPT

US-PAT-NO: 5616342
DOCUMENT-IDENTIFIER: US 5616342 A

TITLE: Emulsioin suitable for administering a poorly water-soluble photosensitizing compound and use thereof

DATE-ISSUED: April 1, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lyons; Robert T.	Cary	NC		

US-CL-CURRENT: 424/450; 514/410

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 4. Document ID: US 5389378 A

L12: Entry 4 of 4 File: USPT

US-PAT-NO: 5389378
DOCUMENT-IDENTIFIER: US 5389378 A

TITLE: Benzoporphyrin vesicles and their use in photodynamic therapy

DATE-ISSUED: February 14, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Madden; Thomas D.	Vancouver			CA

US-CL-CURRENT: 424/450; 428/402.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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Terms	Documents
L11 and (sugar$ or $saccharides)	4

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